Chapter 1
Cancer Immunotherapy:
Beyond Checkpoint Inhibitors

Mohammad Raghibul Hasan
College of Applied Medical Sciences, Shaqra University, Al-Quwayiyah, Saudi Arabia

Bader Saud Alotaibi
College of Applied Medical Sciences, Shaqra University, Al-Quwayiyah, Saudi Arabia

Sultan F. Alnomasy
College of Applied Medical Sciences, Shaqra University, Al-Quwayiyah, Saudi Arabia

Khalid Umar Fakhri
https://orcid.org/0000-0001-6978-8172
Department of Biosciences, Jamia Millia Islamia, New Delhi, India

ABSTRACT

Cancer immunotherapy has become a powerful clinical strategy as well as an established pillar for the treatment of cancers to improving the prognosis of many cancer patients with a broad variety of solid tumors as well as blood cancers. The primary goals of immunotherapy are (a) to increase anti-tumor response, (b) decrease the immune suppression, and (c) to enhance the immunogenicity of tumors. This chapter aims to discuss the mechanism and different types of immunotherapies used for different cancers. It will also focus on recombinant products including immunostimulants, immunotoxins, antibodies, fusion proteins, engineered cytotoxic T cells, engineered immunocytokines, vaccines, checkpoint inhibitors, CAR T-cell therapy, and nanomedicine. Although immunotherapy has a rare side effect, it is not fully understood. The development of new strategies has been on the clinical trial to enhance the benefit of cancer patients to meet with challenges of limited efficacy and/or toxicity.

DOI: 10.4018/978-1-7998-6530-8.ch001

INTRODUCTION

Immunotherapy used to enhance the power of the host immune system for the treatment of malignancies. It has become a powerful clinical strategy for treating and improving the prognosis of many solid and hematological cancer patients. The primary goal of immunotherapy is (a) to increase anti-tumor response, (b) decrease the immune suppression (c), and to enhance the immunogenicity of tumors. Cancer immunotherapy uses recombinant products, including immunostimulants, immunotoxins, monoclonal antibodies, fusion proteins, engineered cytotoxic T cells, engineered immunocytokines, vaccines, checkpoint inhibitors, CAR-T cell therapy, and the nanomedicine. Although immunotherapy has a rare side effect, however, it is not fully understood. The expansion of new strategies has been on the clinical trial to enhance cancer patients' benefit to meet with challenges of limited efficacy and toxicity.

Brief History of Cancer Immunotherapy

Cancer immunotherapy approval started in 1986 with interferon-α2a (IFN-α2a) and IFN-α2b for hairy cell leukemia, Kaposi sarcoma, and other hematological malignancies. In 2012, food and drug administration (FDA) approved Aflibercept due to its use in combination with a chemotherapy regimen (consists of 5-fluorouracil, leucovorin as well as irinotecan) for the metastatic colorectal cancer treatment. New immunotherapy called chimeric antigen receptor-T (CAR-T) cells licensed since 2017, outside clinical trials. The CAR-T cells found with very potent antitumor activity listed in Table 1.

Table 1. CAR-T cells clinical trials

Clinical trial	Patient group	Response rate	Complete remission rate	Overall survival	Reference
ELIANA (Novartis)	Children & young adults with relapsed and refractory B-ALL	81%	81%	Median survival 19.1 months	Maude SL et al., 2018
MSKCC	Adults with relapsed B-ALL	--	83%	Median survival 12.9 months	Park JH et al., 2018
ZUMA-1 (Kite Pharma)	Adults with refractory large B-cell Lymphoma	82%	54%	52% at 18 months	Neelapu SS et al., 2017
JULIET (Novartis)	Adults with relapsed DLBCL or Follicular Lymphoma	64%	43% DLBCL 71% follicular lymphoma	DLBCL median survival 22.2 moths, follicular lymphoma not reached	Schuster SJ et al., 2017
CRB-401 (Celgene/ Bluebird)	Relapsed and refractory multiple myeloma	89%	22%	Not available	Berdeja JG et al., 2017

The Nobel Prize in Chemistry, 2018, awarded jointly to George P. Smith and Gregory P. Winter for the discovery of "phage display of peptides and antibodies," and the other half of Nobel Prize to Frances H. Arnold for the "directed evolution of enzymes." Their pioneer work together utilizes the processes of evolution for the creation of novel biological compounds. These tools transformed the production of pharmaceuticals, such as monoclonal antibodies (mAbs) and renewable fuels. (The Nobel Prize in Chemistry 2018, Frances H. Arnold, George P. Smith, Sir Gregory P. Winter)